REMARKS/ARGUMENTS:

Claims 55-71 are pending in the application. Reexamination and reconsideration of the application, in view of the following remarks, are respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §103:

Claims 55-71 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Applicants' admission on page 7 (first two full paragraphs) of Applicants' response of May 23, 2005, in view of Swayze et al., 6,316,626. The Applicant respectfully traverses this rejection.

Claim 55 is as follows:

> A device comprising a plurality of unmodified biopolymer and a solid support, wherein the solid support has at least one surface comprising pendant acyl fluoride functionalities, and wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl fluoride functionalities, in the absence of a spacer arm.

Applicant respectfully submits that the combination of the Applicants' admission and Swayze cannot render claim 55 obvious, because the Applicants' admission and Swayze fail to teach or suggest a "device comprising a plurality of unmodified biopolymer ... wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl fluoride functionalities, in the absence of a spacer arm."

The Examiner states that since the Applicants have admitted that the invention of attaching unmodified biopolymers to a sold support was known or used by others in this country before the invention thereof by Applicants and since

Swayze teaches the use of acyl fluoride to functionalize a solid support to further attach molecules, the present invention is obvious.

The Applicant respectfully disagrees for the following reasons:

First, contrary to what the Examiner states, the Applicant's statement indicates that it is at least unpredictable prior to the present invention that a biopolymer could be efficiently immobilized directly on a support without modification and without the use of linkers. As acknowledged by the Examiner, the Applicant states (in the response filed May 23, 2005).

> "Prior to the present invention, it was generally understood in the art that the attachment of biopolymers via available terminal amino groups may lead to inefficient and unstable attachment or to reduced activity of the attached biomolecule. Since biopolymers contact supports in a random orientation, the terminal attachment of biopolymers may suffer from low stability and efficiency.
>
> Because of the possible low attachment efficiency and reduction in biomolecule activity of terminal attachments via naturally present amino groups, this methodology has been abandoned years ago in favor of using post-modified or derivatized biomolecules. In view of the state of the art discussed above, prior to the present invention, one skilled in the art could not have predicted with certainty that biopolymers could be efficiently immobilized directly on substrates without modification and without the use of linkers."

Therefore, the Applicant's statement supports the fact that a person of ordinary skill in the art would not think that biopolymers could be efficiently immobilized directly on substrates without modification and without the use of

linkers. If anyone had attempted to attach unmodified biopolymers to a solid support, such attempt was unsuccessful and was abandoned.

The MPEP at 2141.02 states,

> "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention."

Thus, the Applicant's statement as a whole must be considered including portions that would lead away from the claimed invention. The Applicant respectfully submits that the Applicant's statement as a whole indicated that one skilled in the art could not have predicted with certainty that biopolymers could be efficiently immobilized directly on supports without modification and without the use of linkers.

Swayze has no teaching of immobilizing directly the biopolymers to a solid support, and was not relied on by the Examiner for such. Thus, in view of the foregoing, the Applicant respectfully submits that the Examiner has not met the burden of providing a *prima facie* case of obviousness.

> "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the references."
>
> MPEP 2142

In addition, the Applicant respectfully submits that Swayze fails to teach or suggest the use of acyl fluoride to functionalize a solid support to further attach a biopolymer.

Swayze states,

"One feature of the present invention is the use of an amino protecting group to block the reactive amino site or amino combinatorial site on the scaffold. Once the scaffold is attached to the solid support, the amino protecting group can be removed under basic (non-hydrolytic) conditions. The amino group is then derivatized, or functionalized, with the diverse building block or functional group of choice. This building block can be attached to the amino combinatorial site via a variety of linkages including, but not limited to, alkyl, amide, sulfonamide, carbamate, urea, aminoalkane, thiocarbamate, and thiourea. This can be accomplished by choosing the appropriate electrophile to derivatize the amino group. For example, carboxylic acids can be activated using peptide coupling reagents such as EDC, BOP or HATU and reacted with the scaffold nitrogen atom to give amides. Other reagents which can be used include, among others, acid chlorides, acid fluorides, acid imidazolides, acid anhydrides, sulfonyl chlorides, chloroformates, isocyanates, aldehydes (under reductive alkylation conditions), alkyl halides, and isothiocyanates. Thus, each time a specific linkage is desired in a library, it is introduced onto the scaffold via the appropriate coupling conditions using suitable building blocks at the amino combinatorial site." (Swayze, column 24, lines 36-58).

Thus, in Swayze, there are not acyl fluoride functionalities on the solid support. The acyl fluoride, instead, is used as a coupling agent in order to introduce acyl groups onto an amino group on a scaffold. Furthermore, it is the scaffold and not the solid support that reacts with the acyl fluoride.

In light of the foregoing, Applicant respectfully submits that the Applicant's admission and Swayze could not have rendered claim 55 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Claims 56-71 depend from claim 55 and cannot be rendered obvious for at least the same reasons as claim 55. Withdrawal of these rejections is thus respectfully requested.

Claims 55-71 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al., 6,852,487 in view of Swayze et al., 6,316,626. The Applicant respectfully traverses this rejection.

Applicant respectfully submits that the Barany and Swayze cannot render claim 55 obvious, because the combination of references fails to teach or suggest a "device comprising a plurality of unmodified biopolymer ... wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl fluoride functionalities, in the absence of a spacer arm."

The Examiner states that Barany teaches,

> "wherein an unmodified end of the biopolymer is attached to the solid support by reaction with the pendant acyl halide functionalities in the absence of a spacer arm, (col. 26, lines 36-39, and col. 23, lines 20-23, disclosing the attachment of pre-synthesized probes, and col. 32, lines 25-28, disclosing spotting of oligomers to a solid support.)"

The Applicant respectfully disagrees. The sections from Barany, cited by the Examiner, fail to teach or suggest that an unmodified end of a biopolymer is attached to the solid support by reaction with the pendant acyl halide functionalities in the absence of a spacer arm. On the contrary, the experimental details given in Barany teach either the use of modified ends or the use of spacer arms for the attachment of biopolymers.

For example, Barany at column 26, lines 7-20, states,

> "DNA oligonucleotides can be synthesized and terminated with a residue of the amino acid tryptophan, and conjugated efficiently to supports that have been modified by tris(alkoxy)benzyl ester (hypersensitive acid labile ("HAL")) or tris(alkoxy)benzylamide ("PAL") linkers [F. Albericio, et al., J. Org. Chem., 55:3730-3743 (1990); F. Albericio and G. Barany, Tetrahdron Lett., 32:1015-1018 (1991)], which are hereby incorporated by reference). Other potentially rapid chemistries involve reaction of thiols with bromoacetyl or maleimido functions. In one variation, the terminus of amino functionalized DNA is modified by bromoacetic anhydride, and the bromoacetyl function is captured by readily established thiol groups on the support. Alternatively, an N-acetyl, S-tritylcysteine residue coupled to the end of the probe provides, after cleavage and deprotection, a free thiol which can be captured by a maleimido group on the support. As shown in FIG. 12, chemically synthesized probes can be extended, on either end. Further variations of the proposed chemistries are readily envisaged. FIG. 12A shows that an amino group on the probe is modified by bromoacetic anhydride; the bromoacetyl function is captured by a thiol group on the support."

In addition, at column 26, lines 36-47, Barany states,

> "To prepare the arrays of the present invention, the solid supports must be charged with DNA oligonucleotides or PNA oligomers. This is achieved either by attachment of pre-synthesized probes, or by direct assembly and side-chain deprotection (without release of the oligomer) onto the support. Further, the support environment needs to be such as to allow efficient hybridization. Toward this end, two factors may be identified: (i) sufficient hydrophilic character of support material (e.g., PEG or carbohydrate moieties) and (ii) flexible linker arms (e.g., hexaethylene oxide or longer PEG chains) separating the probe from the support backbone."

Therefore, based on the teachings of Barany, a person of ordinary skill in the art would be discouraged from attempting a linkage in the absence of modifying the biopolymer or without the use of a linker arm. Barany, as acknowledged by the

Examiner, fails to teach the use of acyl fluorides and instead, the Examiner relies on Swayze for supplying this teaching. However, as discussed above, the acyl fluoride groups in Swayze are not on the solid support. Instead, the acyl fluoride groups are used as coupling agents in order to introduce acyl groups onto amino groups on a scaffold.

In light of the foregoing, Applicant respectfully submits that the cited references could not have rendered claim 55 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Claims 56-71 depend from claim 55 and cannot be rendered obvious for at least the same reasons as claim 55. Withdrawal of these rejections is thus respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, in view of the foregoing remarks, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (310) 785-4674 to discuss the steps necessary for placing the application in condition for allowance.

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If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
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